Outcomes Assessment

Diabetes Disease Management

Prepared for Kansas Medical Assistance Program in January, 2005

EXECUTIVE SUMMARY

Purpose of Intervention

The primary purpose of this intervention was to determine opportunities for improving the quality and safety of drug therapy for diabetes mellitus following American Diabetes Association guidelines.

Intervention

Intervention Type	Population-based mailing
Intervention Mailing Date	May 2004
Pre-intervention Period (Baseline)	December 2003 – May 2004
Post-intervention Period (Post)	July 2004 – December 2004
Number of Letters Mailed	1,422
Number of Targeted Physicians	1,422
Number of Targeted Patients	5,378
Adjusted Targeted Patients	3,409
Number of Control Physicians	0
Number of Control Patients	0
Adjusted Control Patients	0

Changes in Clinical Indicators

Clinical Indicators	Target		
	Baseline	Dec-04	% Change
Non-Compliance	573	234	-59.2%
Drug-Drug Interactions	116	86	-25.9%
Duplicate Therapy	5	4	-20.0%
Increased Risk of ADE	2,392	1,898	-20.7%
Underutilization	403	267	-33.7%

Savings Calculations

Intervention-Related Drug Therapy	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	$152.31
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	$162.96
Estimated Savings Per Patient Per Month	($10.65)
Total Number of Targeted Patients	3,409
6-Month Total Savings	($217,813.31)

Medical Expenditures	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	$1,174.41
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	$1,077.53
Estimated Savings Per Patient Per Month	$96.88
Total Number of Targeted Patients	3,409
6-Month Total Savings	$1,981,596.37

BACKGROUND

Diabetes mellitus is a heterogenous mix of chronic metabolic disorders characterized by hyperglycemia, which is due to defects in insulin secretion, insulin action, or both. During the past several decades, there has been a significant increase in the prevalence of diabetes. Currently an estimated 17 million people in the United States have diabetes (11.1 million with a diagnosis of diabetes; 5.9 million people estimated to have diabetes, but not yet diagnosed).[1,2] Another 21 million Americans have blood glucose levels higher than the normal range but not yet above the level that defines diabetes. In 2002, the total annual economic costs of diabetes approximated $132 billion. Just over $91.8 billion is attributed to direct medical and treatment costs and $39.8 billion attributed to indirect costs such as disabiity and mortality.[1,2] Serious long-term complications including those resulting from microvascular (small vessel) and macrovascular (large vessel) disease. These include, but are not limited to: blindness, lower extremity amputations, end stage renal disease, heart disease, heart attack, and stroke.

During the past several years there has been a variety new diabetes drug classes introduced to the market. Drug therapy for the management of diabetes historically included only insulin and both first and second-generation sulfonylureas. As of 1995, a variety of new oral antidiabetic medications have been introduced. These include the biguanide class (metformin [Glucophage®, GlucophageXR®]), alpha-glucosidase inhibitors (acarbose [Precose®] and miglitol [Glyset®]), thiazolidinediones (rosiglitazone [Avandia®] and pioglitazone [Actos®]), and the meglitinide class (repaglinide [Prandin®] and nateglinide [Starlix®]). Troglitazone [Rezulin®] was withdrawn from the market in March 2000 due to the risk of severe liver toxicity.[3]

Since the drug classes have different, yet complimentary mechanisms of action to manage diabetes, combination therapy often leads to improved glycemic control. As of August 2000, the FDA approved the first combination product, Glucovance®, a tablet containing a second-generation sulfonylurea, glyburide and the biguanide, metformin.[4] As of late October 2002, two new combination tablets, Avandamet™ (containing rosiglitazoneand metformin) and Metaglip™ (containing glipizide and metformin), were approved by the FDA.[5,6]

In addition to managing the hallmark of diabetes, hyperglycemia, it is also critical to incorporate the management and treatment of associated disorders, such as hypertension, obesity and dyslipidemia. The risk factors identified by the American Diabetes Association (ADA) are listed in the table below. Moreover, these are also risk factors for coronary heart disease. Because of the high mortality rate of diabetic patients with a first myocardial infarction, the American Diabetes Association (ADA) and the National Cholesterol Education Program – Adult Treatment Panel III (NCEP-ATP3) have recommended that dyslipidemia be treated more aggressively (primary goal: LDL cholesterol $\leq$ 100 mg/dL) in patients with diabetes.[7,8] Additionally, low dose enteric-coated aspirin therapy (75-325 mg daily) is recommended as a strategy for both

1 American Diabetes Association. http://diabetes.org. Basic diabetes information. Available via Internet. http://www.diabetes.org/main/. Accessed 05 January 2003.
2 American Diabetes Association. http://diabetes.org. Facts and figures. Available via Internet. http://www.diabetes.org/main/info/facts/facts.jsp. Accessed 05 January 2003.
3 Food and Drug Administration. http://www.fda.gov. Rezulin to be withdrawn from the market. Available via Internet www.fda.gov/bbs/topics/NEWS/NEW00721.html. Accessed 05 November 2002.
4 Glucovance package insert. Princeton, NJ: Bristol-Myers Squibb Company; 2002 October.
5 Avandamet package insert. Research Triangle Park, NC: GlaxoSmithKline; 2002 October.
6 Metaglip package insert. Princeton, NJ: Bristol-Myers Squibb Company; 2002 October.
7 American Diabetes Association. http://diabetes.org. Management of dyslipidemia in adults with diabetes. Diabetes Care. 2003;26(1):83-86.
8 Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285:2486-2497. Full report available at:http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.pdf. Accessed 05 November 2002.

secondary prevention in adult diabetics with evidence of large vessel disease, and as primary prevention for adult diabetics with cardiovascular risk factors.[9,10] Some patients may not be candidates for aspirin therapy. These include patients under the age of 21 years, those with an allergy to aspirin, those with a bleeding tendency or receiving anticoagulant therapy, and patients with active liver disease or who have had a recent gastrointestinal bleed.

[9] American Diabetes Association. http://diabetes.org. Clinical practice recommendations. Diabetes care. 2003; 26(1). Available via Internet. http://care.diabetesjournals.org/content/vol26/suppl_1/**.** Accessed 05 January 2003.
[10] American Diabetes Association. http://diabetes.org. Aspirin therapy in diabetes. Diabetes Care 2003;26(2):87-88.

METHODOLOGY

Changes in prescribing habits for intervention-related drugs were examined. This intervention identified providers whose patients were affected by potential non-compliance, drug-drug interactions, duplicate therapy, underutilization and increased risk of adverse drug events. To assess the impact of the intervention, pharmacy drug claims were reviewed from July 2004 through December 2004.

Clinical Criteria: Criteria, rationale, and text message(s) to providers are listed below. All physicians with at least one recipient "hitting" on criteria received letters.

- Medication Non-Compliance
  This indicator identifies patients taking maintenance diabetes, antihypertensive and antilipemic medications that may be non-compliant with therapy because they have received less than 66% of the cumulative amount prescribed.

  Rationale: Compliance with prescribed maintenance drug regimens is paramount to successful patient outcomes. More than $100 billion is spent yearly for problems related to noncompliance. Over half of written prescriptions are taken incorrectly.[11]

  Sample Provider Paragraph:

  > Your patient may be non-compliant with the identified chronic antilipemic therapy. From prescription data, it appears that your patient received <60 days of maintenance therapy in a 90 day period. Please review this information to determine the best course of action for your patient.

- Drug-Drug Interaction
  The drug-drug interaction indicator identies patients taking antidiabetic agents and/or promotility and who are also taking a prescription medication with a potential interaction.

  Rationale: Patients with potential drug-drug interactions are at increased risk of having an adverse drug event. There may be coordination of care issues if more than one prescriber is involved.

  Sample Provider Paragraph:

  > Azole antifungal-sulfonylurea interaction: Azole antifungals may increase the hypoglycemic effect of sulfonylureas. Please consider an alternative or monitor for signs and symptoms of altered glycemic control, especially when changes in antifungal therapy occur.

- Duplicate Therapy
  The duplicate therapy indicator identifies patients taking at least two different drugs within the same drug class with at least a 35 day overlap in therapy in a 60 day period.

  Rationale: Duplicate within-class drug therapy has not been shown to increase efficacy and may increase the risk of adverse drug events, particularly if coordination of care issues play a role.

[11] Berg JS, Dischler J, Wagner DJ, Raia JJ, Palmer-Shevlin N. Medication compliance: a healthcare problem. Annals of Pharmacotherapy. 1993;27(suppl 9):S1-S19

Sample Provider Paragraph:

It appears that your patient has received the following oral insulin secretagogues concurrently. Use of more than one oral insulin secretagogue is not generally recognized as synergistic and is usually not indicated. Using more than one agent to treat this condition may increase the risk of adverse events (e.g. hypoglycemia) and may decrease overall compliance with prescribed medications. Please review the need for this combination of medications, and if you have not already done so, please verify that your patient has discontinued the appropriate agent(s).

- Underutilization

  Because nephropathy may not routinely be submitted as a diagnosis, this measure identifies patients with a diagnosis of nephropathy, as well as patients without a diagnosis of nephropathy but who have hypertension and diabetes and are not taking an angiotensin modulating agent as potential candidates for either ACE-inhibitor or AIIRA therapy.

  Rationale: Clinical studies have shown that ACE-inhibitors and certain angiotensin II receptor antagoinists (AIIRA) agents (specifically, losartan and irbesartan) decrease or stabilize albuminuria in incipient nephropathy and slow the rate of progression of advanced nephropathy. They should be utilized in all patients with proteinuria, without a contraindication to receiving them, who are type 1 diabetics (normotensive or hypertensive), and hypertensive type 2 diabetic patients.[12,13,14,15,16]

  Sample Provider Paragraph:

  Potential underutilization: Hypertension diagnosis & diabetes medication without an angiotensin-modulating agent. In the absence of contraindications, consider an angiotensin-modulating agent (ACE inhibitor or Angiotensin II Receptor Antagonist) if your patient has incipient or advanced diabetic nephropathy.

- Increased Risk of Adverse Drug Events

  The increased risk of adverse drug event indicator identifies patients receiving medications who are at risk of experiencing an adverse drug event due to predisposing medical conditions. Additionally, certain concomitant medication therapy may result in additive effects resulting in adverse events.

  Rationale: Medication related adverse events are common in primary care, and many are preventable or ameliorable. Improvements in monitoring for and responding to symptoms are especially important for the prevention of adverse drug events in outpatients.

  Sample Provider Paragraph:

  Increased risk of adverse effect: Metformin-Containing Product(s) with hepatic impairment. According to pharmacy and medical claims data, it appears your patient has a diagnosis of hepatic impairment and received a metformin-containing product.

[12] American Diabetes Association. http://diabetes.org. Diabetic nephropathy. Diabetes Care 2003;26(1):94-98.
[13] Remuzzi G, Schieppati A, Ruggenenti P. Nephropathy in patients with type 2 diabetes. N Engl J Med .2002; 346(15): 1145-1151.
[14] Lewis EK, Hunsicker LG, Clarke WR, et.al. Renprotective effect of the angiotensin receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001; 345(12): 851-860.
[15] Brenner BM, Cooper ME, De Zeeuw D, et.al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001; 345(12): 861-869.
[16] Parving HH, Lehnert J, Bröchner-Mortensen J, et.al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. . N Engl J Med. 2001; 345(12): 870-878.

Because hepatic impairment may significantly limit the ability to clear lactate, metformin-containing products should be avoided in patients with clinical or laboratory evidence of hepatic disease due to the increased risk of developing lactic acidosis. Please review the need for this medication, consider the use of appropriate alternatives, or regularly monitor for clinical signs and symptoms of lactic acidosis or worsening of existing hepatic impairment.

Definitions:

Adjusted Target Patients – All patients of physicians who were included in the intervention, who had pharmacy claims and were active plan members throughout the post-intervention time period. Additionally, when outcomes are performed, these patients' pre-intervention (baseline) hits are re-evaluated to make certain that the status of clinical indicators haven't changed for each patient due to late pharmacy and medical claims.

Intervention-Related Drugs – Antidiabetic agents, antihypertensives, and antilipemics.

RESULTS

Characteristics

Table 1 describes the patient population included in the population-based intervention based upon mean age, gender, number of providers, average number of prescriptions per patient per month, and utilization of intervention-related drugs at baseline. As can be seen from the table, the target group had over twice as many females as males, were seeing 3.2 providers, receiving 8.5 prescriptions per month, and taking 4.2 intervention-related drugs.

Table 1: Patient Characteristics

	Target (N=3,409)
Mean Age	**58.2**
Percentage Male	**32.3%**
Percentage Female	**67.7%**
Number of Providers	**3.2**
Average Number of Prescriptions PPPM*	**8.5**
Utilization of Intervention-Related Drugs**	
Average Number of Drugs***	**4.2**
Average Number of Claims	**19.0**
Average Days Supply	**530.7**
Average Amount Paid	**$899.70**

* Number of prescriptions per patient per month (PPPM) is the average for the 6 month baseline period

** Based on 6 months of baseline claims data

*** A distinct drug is defined by using a coding system similar to the Hierarchical Ingredient Code List (HICL) in that distinct drugs are identified at the ingredient level.

Non-Compliance

Table 2 exhibits the incidence of patients identified as being non-compliant with their drug therapy. The intervention saw sizeable reductions in each of the indicators. Overall, a reduction in the non-compliance clinical indicators of 59.2% was achieved during the post-intervention period.

Table 2: Changes in Non-Compliance

Non-Compliance	Target		
	Baseline	Dec-04	% Change
Cardiovascular med, no HTN dx	**44**	**11**	**-75.0%**
Antidiabetics	**171**	**71**	**-58.5%**
Antilipemics	**68**	**25**	**-63.2%**
HTN med & dx = HTN	**290**	**127**	**-56.2%**
Total	**573**	**234**	**-59.2%**

Drug-Drug Interactions

Table 3 represents the incidence of patients identified as having drug-drug interactions. Overall, a reduction in the drug-drug interaction clinical indicators of 25.9% was achieved during the post-intervention period.

Table 3: Changes in Drug-Drug Interactions

Drug-Drug Interactions	Target		
	Baseline	Dec-04	% Change
Sulfonylurea-Azole antifungals	5	4	-20.0%
Sulfonylurea-Cyclosporine, >1 MD	3	1	-66.7%
Sulfonylurea-Salicylates	3	1	-66.7%
Sulfonylurea-Sulfonamide	9	6	-33.3%
Sulfonylurea-Warfarin	96	74	-22.9%
Total	116	86	-25.9%

Duplicate Therapy

The change in the number of patients identified as having duplicate therapy is presented in Table 4. Overall, a reduction of 20.0% was achieved during the post-intervention period.

Table 4: Changes in Duplicate Therapy

Duplicate Therapy	Target		
	Baseline	Dec-04	% Change
Oral Insulin Secretagogues	5	4	-20.0%

Underutilization

Table 5 exhibits the incidence of patients identified as underutilizing therapy. Overall, a reduction in underutilization clinical indicators of 33.7% was achieved during the post-intervention period.

Table 5: Changes in Underutilization

Underutilization	Target		
	Baseline	Dec-04	% Change
Diabetes Meds & HTN Dx: no angiotensin-modulating agent	24	13	-45.8%
Diabetes & HTN Diagnosis: no angiotensin-modulating agent	379	254	-33.0%
Total	403	267	-33.7%

Increased Risk of ADE

Table 6 exhibits the changes in the number of patients identified as being at an increased risk of ADE. Overall, a reduction in the increased risk of ADE clinical indicators of 20.7% was achieved during the post-intervention period.

Table 6: Changes in Risk of ADE

Increased Risk of ADE	Baseline	Target Dec-04	% Change
Metformin Product(s) with Hepatic impairment	17	11	-35.3%
Metformin Product(s) with Renal Impairment	36	21	-41.7%
Geriatric: Increased risk of ADE: Metformin Product(s)	114	88	-22.8%
Metformin-Containing Product(s) with Heart Failure	246	178	-27.6%
Metformin Product(s) with Inferred Heart Failure	35	25	-28.6%
Chlorpropamide, age > 70	1	1	0.0%
Alpha-glucosidase inhibitors & GI disease	2	0	-100.0%
Thiazolidinediones & Liver Disease	5	4	-20.0%
Thiazolidinediones & HF DX	132	101	-23.5%
Diabetes Dx No Microalbumin in 550d	287	227	-20.9%
Diabetes Dx No Fasting Lipid Panel in 550d	212	160	-24.5%
Diabetes Dx <2 Hemoglobin A1C labs in 550d	1,250	1,048	-16.2%
Rosiglitazone-Metformin with Heart Failure Dx	10	5	-50.0%
Rosiglitazone-Metformin w/Inferred Heart Failure	1	1	0.0%
Metformin-Containing Product(s) with H/O Acidosis	27	16	-40.7%
Diabetes Dx: No eye exam within last 550d	17	12	-29.4%
Total	2,392	1,898	-20.7%

The overall savings for the intervention are calculated in Tables 7 and 8. Per patient per month (PPPM) drug amount paid for intervention-related drugs and medical claims were separately calculated for the target group for the six-month baseline and six-month post-intervention periods. The post-period PPPM amount paid for the target group was subtracted from the baseline PPPM amount paid to obtain the estimated PPPM savings. The PPPM savings was then multiplied by the number of intervention months and number of target patients.

As would be expected from the decrease in underutilization and the large increase in compliance seen in the clinical analysis, Table 7 shows the amount paid for intervention-related drugs increased $10.65 in the post-intervention period. This yielded an overall increase of $217,813 in intervention-related drug expenditures during the six-month post-intervention period.

As seen in Table 8, as a result of the intervention, the estimated per patient per month savings for intervention-related medical claims was $96.88. This yields an overall medical savings of $1,981,596 during the six-month post-intervention period.

Table 7: Intervention-Related Drug Savings

Savings Calculation:	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	$152.31
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	$162.96
% Change in Target Group from Baseline to Post	6.99%
Estimated Savings Per Patient Per Month	($10.65)
Total Number of Targeted Patients	3,409
6-Month Total Savings	($217,813.31)

Table 8: Intervention-Related Medical Savings

Savings Calculation:	
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Baseline)	$1,174.41
Targeted Group: Actual Average Paid Amount Per Patient Per Month (Post)	$1,077.53
% Change in Target Group from Baseline to Post	-8.25%
Estimated Savings Per Patient Per Month	$96.88
Total Number of Targeted Patients	3,409
6-Month Total Savings	$1,981,596.37

LIMITATIONS

A control group was not utilized for this intervention. This limited the comparisons that could be performed in the analysis. Therefore, instead of being able to compare an intervention group with a non-intervention group, the analysis is essentially limited to changes in the intervention group before and after intervention.

The time frame of 6 months may not capture the full extent of the impact of the diabetes intervention. Providers may be required some time before they can change their patient's drug regimens.

CONCLUSIONS

This diabetes disease management intervention focused on improving prescribing practices and reducing the overall cost of care. The intervention was successful in reducing the target patients flagged for non-compliance by 59.2%, drug-drug interactions by 25.9%, duplicate therapy by 20.0%, underutilization by 33.7%, and increased risk of ADE by 20.7%.

As would be expected from the large increase in compliance and the decrease in underutilization seen in the clinical analysis, the amount paid for intervention-related drugs increased $10.65 in the post-intervention period. This yielded an overall increase of $217,813 in intervention-related drug expenditures during the six-month post-intervention period. However, as a result of the intervention, the estimated paid amount per patient per month for intervention-related medical claims decreased $96.88. This yields an overall intervention-related medical savings of $1,981,596 during the six-month post-intervention period. Therefore, the total savings due to the intervention was $1,763,783 during the six-month post-intervention period.